

### **REMARKS**

Claims 1, 15-20, and 22-25 are currently pending in this application. Claims 1, 15-20, and 22-25 stand rejected on arguments laid out in the Office Action mailed on December 31, 2007. Claims 1, 16, and 20 have been amended. Claim 25 has been canceled by the present amendment. No new claims have been added.

Applicant would first like to thank Examiner Chen for taking time to discuss the outstanding rejections with Applicant's representatives during a phone interview on January 16, 2008. In particular, the topic of enablement for a method of delivery by chlorotoxin was discussed. The Examiner indicated that his concern was that the claims read as a method of treatment rather than of delivery because of the references to a "pharmaceutical composition" and to "an effective dose."

Claim 1 has now been amended to remove references to "pharmaceutical composition" and "effective dose."

Claim 16 has been amended to remove reference to a tumor type "treated."

Claim 20 has been amended to remove an inadvertent typographical error that resulted in repetition of the phrase "selected from."

Claim 25 has been canceled without prejudice.

Applicant submits that no new matter is introduced by these amendments.

Applicant respectfully requests reexamination and reconsideration of the case, as amended. The current amendments to the claims obviate the rejections levied in the Office Action mailed on December 31, 2007. Nevertheless, each of the rejections levied in the Office Action is addressed below.

#### **Claim objections:**

The Examiner has objected to claim 20 because of the informality of having "selected from" twice in the claim. Claim 20 has been amended in light of Examiner's objection. Applicant hereby requests removal of this objection.

Claim rejections under 35 U.S.C. § 112:

Claim 16 stands rejected under 35 U.S.C. § 112, second paragraph. In particular, the Office Action points out that the term “treated” in the phrase “wherein the neuroectodermal tumor is a tumor type treated” lacks sufficient antecedent basis. Applicant has amended claim 16 to remove the term “treated,” thus rendering this rejection moot.

Claims 1, 15-20 and 22-25 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. In particular, the Office Action takes the position that “the specification, while being enabling for delivering chlorotoxin fused to a cytotoxic moiety to neuroectodermal tumors *in vitro* does not reasonably provide enablement for delivering a cytotoxic moiety to a neuroectodermal tumor *in vivo*...”

In the phone interview of January 16, 2008 the Examiner clarified that this rejection arises from the phrases “pharmaceutical composition” and “effective dose,” which the Examiner feels imply a method of treatment, and indicated that his concern was with an implication of successful *treatment*.

Solely in order to advance prosecution of the present case, Applicant has amended independent claim 1 such that it no longer refers to a “pharmaceutical composition” or “effective dose.” Similarly, Applicant has canceled claim 25 without prejudice. Claim 25 depends on claim 1 and cites that the dose of chlorotoxin is effective to reduce the size of the tumor.

Applicant nevertheless reiterates all prior arguments in this regard and again points out that the specification is fully enabling for a method of delivering a cytotoxic moiety to a neuroectodermal tumor *in vivo* as well as *in vitro* (and indeed is enabling for a method of treatment). Applicant reiterates that the specification incorporates by reference the entire content of the two applications to which the present application claims priority (i.e. Application 08/774,154, which issued as U.S. Patent 5,905,027 and Application 09/296,031, which issued as U.S. Patent 6,667,156). Thus, the present application incorporates by reference the *in vivo* and other data presented in the U.S. Patents 5,905,027 and 6,667,156. Example 17 of U.S. Patent 5,905,027 shows that injection of <sup>131</sup>I-TM-601 (a chemically synthesized form of chlorotoxin

covalently linked to iodine 131) into the cerebrum of a mouse bearing a glioma results in tumor-selective uptake of <sup>131</sup>I-TM-601.

Though the presently amended claims do not require successful treatment, Applicant argues that the specification supports such a method. Example 23 of U.S. Patent Number 5,905,027 shows that treating glioma cells with a chlorotoxin-GST fusion protein attached to saporin (a cytotoxic moiety) results in significant and selective killing of the glioma cells. Combined with the results described in Example 17 of U.S. Patent Number 5,905,027, these results support enablement for a method of treatment.

Furthermore, Applicant has presented in a Declaration by Dr. Alison O'Neill (filed May 21, 2007) evidence of delivery of a cytotoxic moiety using a chlorotoxin agent *in vivo*. This Declaration presents results of clinical trials using <sup>131</sup>I-TM-601 in human patients with recurrent high-grade glioma. The results show that a chlorotoxin-cytotoxic moiety complex (1) selectively reaches its target tumor site when administered to a patient either through intracranial or intravenous administration; (2) passes through the blood-brain barrier to reach a tumor located in the brain; and (3) has a therapeutic effect *in vivo*. Intravenous administration of the chlorotoxin complex resulted in selective uptake in glioma and metastatic melanoma, two neuroectodermally-derived tumors.

Though Applicant has provided evidence that the present specification not only enables a method of delivery *in vivo* as well as a method of treatment *in vivo*, Applicant has amended independent claim 1 to remove references to "pharmaceutical composition" and an "effective dose." These amendments render the rejection moot. Applicant hereby requests that the rejection be withdrawn.

### CONCLUSION

Applicant again thanks the Examiner for his careful review of the case. The claims have been amended to obviate all rejections. Based on the Remarks presented above, Applicant respectfully submits that Claims 1, 15-20, and 22-24 are now in condition for allowance. A Notice to this effect is respectfully requested.

Please charge any fees that may be associated with this matter, or credit any overpayments, to our Deposit Account No.: 03-1721.

Respectfully submitted,

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